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Award Number: W81XWH-07-1-0282

TITLE: Identifying and Overcoming Barriers to Diabetes Management in the Elderly: An Intervention Study

PRINCIPAL INVESTIGATOR: Dr. Medha Munshi

CONTRACTING ORGANIZATION: Joslin Diabetes Center, Inc.
Boston, MA 02215

REPORT DATE: June 2011

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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REPORT DOCUMENTATION PAGE				<i>Form Approved</i> OMB No. 0704-0188	
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1. REPORT DATE (DD-MM-YYYY) 01-06-2011		2. REPORT TYPE Final		3. DATES COVERED (From - To) 1 JUN 2007 - 31 MAY 2011	
4. TITLE AND SUBTITLE Identifying and Overcoming Barriers to Diabetes Management in the Elderly: An Intervention Study				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER W81XWH-07-1-0282	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Dr. Medha Munshi E-Mail: medha.munshi@joslin.harvard.edu				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Joslin Diabetes Center, Inc. Boston, MA 02215				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT In this randomized controlled study, we evaluated the effect of assessment and intervention for age-specific barriers, on the glycemic control and other clinical, functional and psychosocial parameters in 100 subjects over the age of 69 years with poorly controlled diabetes. The intervention group had an assessment of age-specific barriers followed by designing strategies to improve their ability to follow diabetes management plans as prescribed by their providers. The interventions were implemented by a care manager in half subjects and via phone calls from the office in the other half of the group. The attention control subjects received equal number of "courtesy" phone calls by an educator. All subjects underwent measurement of glycemic control (A1C) and other outcome measures at baseline and 6-months. Second assessment of outcome measures was performed in all patients at 12-months from baseline (after 6 months of no contact with study team) to assess if changes during intervention were sustained. The important results show 1) there are many barriers to self-care in older adults. 2) Phone communication between clinic visits by an educator improves glycemic control and lowers diabetes-related distress 3) Communication with an educator cognizant of age-specific barriers may improve glycemic control more and help maintain functionality 4) Hypoglycemic episodes are common in even in poorly controlled older patients on insulin regimen.					
15. SUBJECT TERMS Diabetes, Elderly, Glycemic control, Continuous glucose monitoring, Hypoglycemia, Care management					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 38	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			19b. TELEPHONE NUMBER (include area code)

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Introduction:

In this project we studied special challenges faced by elderly patients with diabetes and evaluated ways to help patients overcome these barriers.

Diabetes Mellitus is a major public health problem affecting an increasing number of older individuals. Burdened with additional medical, functional, and psychosocial issues, many older adults struggle to follow their diabetes treatment regimen. When the same criteria and strategies to manage diabetes in young adults are applied to the elderly without considering their special circumstances, there is an increased risk of 1) noncompliance 2) complications of treatment e.g. hypoglycemia or falls, and 3) poor glycemic control leading to complications.

In this study, we evaluated whether short-term focused intervention by a geriatric multidisciplinary team with the addition of a geriatric life specialist is superior to usual care (with attention control) in improving glycemic, functional, economic and quality of life parameters in elderly patients with diabetes, and whether these interventions have persistent effects on outcome measures. In addition, we also assessed changes in cerebral perfusion in elderly with type 2 diabetes following six months intervention and assess whether changes in cerebral perfusion persist at a one-year follow up. We recruited patients over age 70 with diabetes and randomized them to care by either geriatric diabetes intervention team (GDT) or attention control group. Subjects in GDT group had comprehensive geriatric assessment and have individualized intervention performed with help of a geriatric life specialist. Intervention by GDT included focused strategies to overcome barriers in the areas of clinical care, education, social environment, and finances. At the end of 6 months of intervention, the goal was to develop a support network that may empower patients to sustain improvements seen during the intervention. After 6 months of independence period (no contact from GDT), outcome parameters were measured again to see if improvement at 6 months was sustained after 12 months. The subjects in the control group had similar contact time as the GDT group, but with a research team without geriatric expertise. Improvement in clinical, functional, quality of life and economical outcome measures in both groups were compared at 6 and 12 months intervals. At these time points (0, 6 and 12 months) patients were also evaluated for effect of improved glycemic control on cerebral perfusion and glycemic excursions.

Project Tasks:

Task 1: Program Set-up & training and recruitment of study subjects (Mos. 0-36): at Joslin Clinic

Program development, recruitment of geriatric life specialist and training of the geriatric life specialist (Mos. 0-12)

Over the first 0-6 months of the study, we developed detailed project procedures and recruited and trained various personnel including research assistant, diabetes educator, nutritionist, and geriatric life specialist. At the same time, all the institutional approvals were obtained which took longer than expected as we had to go through 2 committees on human studies; at the Joslin Diabetes Center as well as at the Beth Israel Deaconess Medical Center (BIDMC).

We then worked with Human Research Protection office (HRPO) at the USAMRMC, to modify our protocol for compliance with applicable federal, DOD, and Army human subjects protection regulations. As per the suggestions by the Human Subject Protection Scientist at the HRPO, we designed detailed protocol procedures for the intervention group as well as attention control group. We designed telephone dialogue scripts, brochures and fliers for the study recruitment process. We also modified the protocol, consent forms and assent form as recommended. We described, developed and/or modified many of the outcome measurement tools for clinical, functional and psychosocial parameters. Simultaneously, we developed database with forms and data management tools.

Identification of study subjects from electronic medical records and recruitment (Mos. 3-36)

As mentioned above, our recruitment started a little later than expected in the third quarter of the study due to lengthy approval process that we needed to go through. Once the approvals were received, we initially focused our attention on the Joslin clinic population. We have an excellent system to identify eligible subject from medical records at the Joslin diabetes center. We called/screened numerous eligible patients. However, recruitment during winter season in Massachusetts was difficult. Frequent inclement weather caused many study visit cancellations in the elderly patients with diabetes, also affecting accrual to the study. To modify this situation, and to increase our recruitment pool, we submitted our study protocol for approval at the Beth Israel Deaconess Medical Center. We received approval from the human subject protection committee at BIDMC, and submitted the protocol changes to the HPRO at the USAMRMC. Besides adding this center to improve enrollment, we have also encouraged different ways to facilitate transportation in elderly patients. These measures improved enrollment.

At the end of the study, we have recruited total of 100 older patients with diabetes; 16 patients in the control group and 35 patients in the geriatric life specialist intervention group for this study. Additionally, we have studied 49 more subjects for a parallel study. Thus our final analysis includes 30 patients in the control group, 35 patients in the geriatric life specialist intervention group and 35 patients with similar intervention without geriatric life specialist.

Task 2: Baseline assessment (Mos. 4-36): at Joslin Clinic

We have collected extensive data in our clinical and functional assessment at baseline. Following surveys and tools were completed at the baseline, at 6-months and at 12-months visits:

1. Demographics and Medical history form
2. Healthcare utilization form
3. hypoglycemia history form
4. medications adherence assessment
5. Functional assessment by
 - a. ADL
 - b. IADL
 - c. 6-minute walk test
 - d. Tinetti assessment for gait and balance
6. Cognitive function tests
 - a. Trail making test-A and B
 - b. Clock-in-a-box test
 - c. Verbal fluency test
7. Depression screening
 - a. Geriatric Depression Scale
8. Assessment of diabetes-related distress with help of
 - a. PAID (Problem Areas In Diabetes)
9. Nutrition assessment
 - a. DETERMINE nutrition test
10. Self-care inventory 2
11. Assessment of social support
 - a. Older American Resource and Services (OARS)
12. Care-giver burden interview

In addition, in the second year of the study, based on our experience with the study subjects and based on the recent publication of an article, we added continuous glucose monitoring to our protocol for assessment of glucose excursion in older patients. We renegotiated the budget and applied and receive regulatory approvals from all institutional entities. This provided very important data not available in literature for better diabetes care in older adults and has already resulted in publication.

As we collected baseline data, we performed cross-sectional interim analysis and submitted abstracts to the scientific meetings of the American Diabetes Association over last 3 years. They were presented at the meeting as posters and oral presentations. The abstracts showing baseline data are as follows.

Results:

1. Higher Exercise Capacity in Older Adults with Diabetes is Associated with Better Self-Care Ability and Less Diabetes-Related Stress. In: 69th annual meeting of the American Diabetes Association; New Orleans La; 2009. 367-OR

Diabetes in older adults is associated with multiple co-existing medical conditions that increase the overall burden of self-care and affect quality of life. Exercise is an integral part of diabetes management for all patients but its effect on self-care ability and diabetes related stress in older adults is not well studied.

Methods: Community-living adults ≥ 70 years, A1c $>8\%$, were enrolled in a study to identify geriatric-specific barriers to diabetes management. Exercise capacity was tested using the 6-Minute Walk Test (6MWT). Self-care ability and diabetes-related stress were evaluated using Self-Care Inventory (SCI) and Problem Areas in Diabetes (PAID) questionnaires respectively. Subjects were also assessed for cognitive dysfunction, depression, and glycemic control (A1c).

Results: Forty-five subjects (age 76 ± 5 years, diabetes duration 22 ± 10 years) were divided into 2 groups based on distance walked during 6MWT at median value (313 meters). Subjects with higher exercise capacity tended to be male (77% vs 48%, $p < 0.05$), Caucasian (91% vs 50%, $p < 0.002$), and had lower BMI (31 ± 6 vs 35 ± 9 , $p < 0.04$). This group scored higher on SCI (67 ± 9 vs 56 ± 14 , $p < 0.003$) suggesting better self-care abilities and lower on PAID (18 ± 10 vs 30 ± 16 , $p < 0.006$) reflecting less diabetes related stress, compared to subjects with lower exercise capacity. Depressive symptoms (measured by Geriatric Depression scale) were present in 18% of the subjects in the lower exercise capacity group as compared to none in high scoring group ($p < 0.03$). Groups did not differ with respect to A1c and measures of cognitive function. However, the higher exercise group had better gait and balance (Tinnetti score 26 ± 2 vs 22 ± 7 , $p < 0.004$) and was more likely to be independent in performing activities of daily living (IADL score 16 ± 0.8 vs 14 ± 3 , $p < 0.04$).

Conclusions: Higher exercise capacity is associated with better self-care ability, less depression, less diabetes-related stress and better performance of daily tasks. Exercise education should be stressed in older adults with diabetes to maintain functional independence and optimize quality of life.

2. The risk of hypoglycemia is a treatment-limiting factor in older adults even with poor glycemic control. In: 69th annual meeting of the American Diabetes Association; New Orleans La; 2009. 2123-Po

In older adults with diabetes, hypoglycemia is the most important factor limiting efforts to improve glycemic control. The efforts to avoid hypoglycemia may lead to poor glycemic control in these patients. Occurrence and frequency of episodes of hypoglycemia in this population with inadequate glycemic control remains unknown.

Methods: Patients > 70 years of age with poor glycemic control ($A1c > 8\%$), enrolled in a study to identify barriers to diabetes management were evaluated for hypoglycemic events. A detailed questionnaire was administered to characterize hypoglycemia. Demographic information and clinical data were collected by surveys. All of the subjects underwent testing for cognitive function, depression, and functionality.

Results: We evaluated 45 patients with average age 75 ± 5 years, duration of diabetes 22 ± 10 years, and $A1c$ $9.1 \pm 0.5\%$. Over 90% patients were receiving insulin in this group. Despite poor glycemic control, 42 of 45 patients reported episodes of hypoglycemia within past 3 months. Eighteen of forty-two (43%) subjects had frequency of more than few episodes a month, while 57% had rare episodes. Cognitive dysfunction was identified in 28% patients with high frequency and 33% patients with low frequency of hypoglycemia ($p = NS$) suggesting possibility of under-reporting of this condition. In patients with higher frequency of hypoglycemia $A1c$ was lower (8.8 ± 0.5 vs 9.5 ± 1 ; $p < 0.01$) suggesting wide glycemic excursions. Although typical hypoglycemic symptoms such as shakiness (56%) and sweating (51%) were frequently reported, atypical symptoms such as weakness (31%), hunger (31%), change in behavior (16%) dizziness (16%), and vision changes (18%) were also common, and can be missed if not asked for specifically. Twenty four (53%) patients continued to drive but only 11 (24%) patients checked blood glucose before driving. Only 36% patients with hypoglycemia reported fear of hypoglycemia.

Hypoglycemia should be carefully looked for even with poor glycemic control in the older population. Improvement of glycemic control may require improving wide glucose excursions in this population.

3. Inadequate social resources is associated with increased clinical, functional and economic burden in older adults. In: 69th annual meeting of the American Diabetes Association; New Orleans La; 2009; 1870-P.

Managing diabetes in older adults is complicated by co-existing medical, functional and psychosocial issues. The effect of the availability of social resources on these aspects in older adults with diabetes is not well studied

Methods: We evaluated patients >70 years age with poor glycemic control (A1C>8%) enrolled in a study to assess the barriers to diabetes management for the effect of available social resources on clinical, functional and economic burden. Social resources were assessed by OARS (Older American Resource and Services), a tool developed by the Duke OARS program to assess the availability of physical and emotional resources. A maximum score of 14 reflected excellent availability of social resources. The subjects were divided into low vs high resources groups at the mean OARS score of 12. All of the subjects were tested for cognitive dysfunction, depression, and functionality. Data on overall health and health services utilization were collected by administering questionnaires.

Results: Forty-five patients with diabetes were evaluated. Eighteen of 45 (40%) subjects had a low score on OARS compared to 27/45 (60%) with high score. Age was similar in both groups (76± 6 vs 76±4 years). Compared to subjects in the high resource group, low social resource group tended to be female (83% vs 48%, $p<0.01$), had longer duration of diabetes (25 vs 18 years, $p<0.03$) and lived alone (56% vs 19%, $p<0.009$). In addition, the group with low social resources had higher A1c (9.4 ± 1.2 vs 8.9 ± 0.5 , $p<0.05$) indicating poor glycemic control, lower exercise capacity as measured by lower score on 6 minutes walk test (235 vs 364 meters), and higher number of ER visits in past 3 months (44% vs 15%, $p<0.04$) suggesting higher healthcare costs, compared to the higher social support group. There was no difference between the 2 groups in the areas of cognitive function, depression, stress related to diabetes management or self-care abilities

Conclusions: In older adults with diabetes, inadequate social resources are associated with poor glycemic control, lower functionality and higher health care cost. It is important to assess individual older adults' resources while providing management plans.

Task 3: Team assessment and active intervention by Geriatric care ambassador (geriatric life specialist (GLS) (mos. 4-42) at Joslin Clinic

Each patient in the intervention group underwent multidisciplinary assessment by the team consisting of a geriatric diabetologist, a nurse educator and a nutritionist. The list of assessments (Table 1) and the interventions recommended (Table 2) are shown below.

Barrier Assessment
<u>In adequate medications</u> -not adequate titrating -unable to get provider appointment -too complicated regimen to follow
<u>Inadequate nutritional information</u>
<u>Inadequate physical activity</u>
<u>Lack of diabetes-related information</u> -inadequate previous education -low health literacy
<u>Presence of co-morbidities interfering with self-care</u> -cognitive dysfunction -depression -visual impairment -auditory impairment -mobility/dexterity issues -swallowing problems
<u>Hypoglycemia and fear of hypoglycemia</u>
<u>Social barriers</u> -isolation - transportation difficulties -lack of motivation -caregiver stress -financial difficulties -major events self/family members interfering with self-care -difficulty with care coordination and facilitation
<u>Behavioral issues</u> -inadequate medical visits -inadequate monitoring -not integrating recommendations from providers -health beliefs interfering with therapy

Interventions
<u>Referral for diabetes education</u> -regarding treatment regimen
<u>Earlier appointment with medical provider</u> -with MD/nurse practitioners -with primary care providers
<u>Referral for Nutritionist</u> -dietary counseling
<u>Referral for exercise</u> -referral for exercise physiologist, physical therapy -community exercise programs -home exercise programs
<u>Diabetes related brief education, assistance, practical tips for better adherence</u> -reinforcing information given by medical providers -assistance with BG monitoring, meter use, schedule set up -recommend and set up assistive devices including reminders for meals and monitoring, vision, gait - hypoglycemia education/reeducation -recommend referral to audiology
<u>Coping with co morbid conditions</u> -referral to memory clinic -referral to mental health clinic -cognitive aids -recommended referral to ophthalmology, podiatry
<u>Help to utilize community resources</u> -health care services -patient/public assistance programs -social services -transportation
<u>Medication related assistance</u> -help with discount meds -set up pharmacy delivery -set up medication adherence aids -pharmacy assistance programs

Over the study period, we continued interim analysis of the data collected and submitted this data as abstracts at the scientific meetings of the American Diabetes Association. The abstracts were presented as poster or oral presentation.

1. Unrecognized errors in insulin injection techniques are frequent in older adults even with longer duration of insulin use. In: 69th annual meeting of the American Diabetes Association; New Orleans La; 2009; 913-P.

Co-existing medical conditions such as cognitive dysfunction and vision/hearing problems are common in older adults and may interfere with their ability to perform self-care. Insulin injections pose a particularly difficult problem.

Methods: As part of an ongoing study to assess barriers to diabetes management in older adults, an in-depth diabetes self-management assessment was conducted on 27 community living older adults (age 76.4 ± 5.1 years, duration of diabetes 17.8 ± 9.1 years). Twenty-two of 27 (81.4 %) subjects were on insulin. Study participants on insulin were questioned about their insulin use and observed drawing or dialing up their insulin doses.

Results: When interviewed, none of the participants reported any trouble taking their insulin, however, when observed by a certified diabetes educator, 12/22 insulin users (54%), with long duration of insulin use (average 13.1 years) were found to have difficulty with technique or dosing. Problems with technique included difficulty seeing the lines on the syringe, mixing the insulin correctly, seeing air in the syringe and inability to follow the steps correctly. Problems with dosing included taking too much or too little, not understanding regimen, and reports of omitting insulin. The group having trouble with insulin technique and dosing were more likely to miss doses of other medications ($p=0.009$) suggesting overall problems with adherence, and were having trouble reading food labels ($p=0.05$) suggesting possible problems with health literacy. Higher frequency of falls, fear of falls, and difficulty walking were more common in the group having problems taking insulin, however, these parameters did not reach statistical significance. There were no differences between the two groups in areas of glycemic control ($A1c$ 9.5 vs 9.1%), vision, cognitive function, depression, or diabetes related stress.

Conclusions: Observing insulin technique periodically should be an important part of the diabetes assessment in older adults even with a long duration of insulin use. Assessment of co-existing medical condition should be integrated in education regarding insulin injections.

2. Frequent hypoglycemia among older adults with $A1c > 8\%$ detected by continuous glucose monitoring. 70th annual meeting of the American Diabetes Association; Orlando FL; 2010. O123-OR

Burdened with medical and functional co-morbidities, older adults with diabetes struggle to achieve glycemic control, often resulting in increased risk of hypoglycemia. Episodes of hypoglycemia are particularly dangerous in the older population. To reduce the risk of hypoglycemia, relaxation of the standard $A1c$ goal to $< 8\%$ has been proposed for the frail elderly. However, the effectiveness of this recommendation in reducing hypoglycemia is unknown.

Methods: We evaluated community-living adults age ≥ 70 years, with $A1c > 8\%$, for episodes of hypoglycemia. We used blinded continuous glucose monitoring (CGM) for at least 72 consecutive hours. Patients performed finger-stick monitoring 4 times a day during CGM use and documented symptoms suggestive of hypoglycemia.

Results: CGM was performed on 33 adults for a mean duration of 87.7 hours. Mean age of the population was 75.2 ± 4.6 years, duration of diabetes 18.6 ± 11 years, and $A1c$ $9.4 \pm 1.3\%$. Seventy-seven percent of patients had type 2 diabetes and 91% were using insulin. At least 1 episode of hypoglycemia (glucose < 70 mg/dl) per CGM period was observed in 20 patients (61%), with mean glucose level of 61 ± 6.2 mg/dl during the

episode. The average number of hypoglycemic episodes was 3.85/patient and average duration was 53 minutes/episode. Eighty percent of patients with hypoglycemia (16/20) suffered at least 1 nocturnal episode (between 10 pm-6 am), with average duration of 52.5 minutes/episode. Out of a total of 77 hypoglycemic episodes, 73 (95%) were unrecognized (not captured by either finger-stick monitoring or by subjective symptoms). All patients with hypoglycemia had at least 1 unrecognized hypoglycemic episode. Only 1/32 nocturnal episodes was recognized by patients. Fifty percent (10/20) of the patients with hypoglycemia had an A1c >9% and 60% (6/10) of these patients had nocturnal hypoglycemic episodes.

Conclusions: We conclude that hypoglycemia, especially unrecognized hypoglycemia, is common in older adults, even in those with high A1c levels. This suggests that simply relaxing the standard A1c goal to <8% will not be sufficient to reduce the incidence of hypoglycemia to an acceptable safe level for the frail elderly population with diabetes.

Task 4: Outcome parameters assessment and start of independence period (Mos. 10-47):

During the study, we identified continuous glucose monitoring (CGM) as a tool for pattern identification and for recognizing hypoglycemia in this elderly population. We asked for an addendum to the protocol to perform CGM at baseline, 6-months and 12-months. We received approval from all institution approval committees. This assessment has already resulted in a publication in the prestigious journal "The Archives of Internal Medicine".

We have 99 % completion rate for 6-month assessment for the glycemic control. Older adults with diabetes with poor control are a very frail and vulnerable population and there are many challenges to performing 12-months longitudinal study on that population. Some patients could not complete functional and psychosocial assessment tools at 6-months due to illnesses. We believe that our diligent follow-up resulted in excellent completion rate in this difficult population.

Our interim data analysis was presented at the scientific meeting of the American Diabetes Association.

1. Self-management interventions to overcome barriers to diabetes care in older adults: A randomized controlled study. 70th annual meeting of the American Diabetes Association; Orlando FL; 2010. 0716-P

Older adults with diabetes face adverse clinical, functional and psychosocial challenges to diabetes self-management. We performed a randomized controlled study to assess whether geriatric-specific intervention strategies can help older adults achieve better glycemic control and improve ability to perform self-care. Methods: We randomized adults ≥ 70 years age with diabetes for ≥ 1 year, with $A1C > 8\%$, to either an intervention or a control group. After baseline assessment of outcome measures, the intervention group had geriatric team evaluation and interventions to optimize their ability to follow diabetes treatment regimen. The attention control group received equivalent time from a separate research staff. Diabetes providers followed all patients for medication management. All patients underwent clinical [A1c, body mass index (BMI)], functional [Instrumental activities of daily living (IADL), and Tinetti Test for gait and balance], and psychosocial [self-care abilities (Self Care Inventory-revised (SCI)) and diabetes-related distress (Problem Areas in Diabetes (PAID))] assessments at baseline and 6 months.

Results: To date, 58/90 (64%) of the patients (average age 76 ± 5 years, diabetes duration 21 ± 12 years, $A1c$ $9.2 \pm 1.1\%$, BMI 33 ± 7 , 71% type 2, and 93% on insulin therapy) completed 6 months intervention. The most common barriers found were need for diet counseling (88%), medication adjustment (85%) and inadequate exercise (60%). The most common interventions were referral to nutritionist (90%), referral to educator (88%) and earlier appointment with medical provider for medication adjustment (68%). As shown in the table, the intervention arm improved on Tinetti, SCI, PAID, BMI and A1c, while IADL deteriorated in the control arm.

Conclusion: Focused geriatric specific interventions improve diabetes management capability in older adults.

Change from baseline to 6 months	Attention Control N= 18	Intervention N= 40
Tinetti Test*	-2.5 \pm 5 (p=NS)	1.3 \pm 3 (p=0.009)
SCI	1.57 \pm 10 (P =NS)	6.9 \pm 10.3 (p=0.0002)

PAID	-3.5±10 (p=NS)	-5.6±15 (p=0.03)
BMI	-2.9±8. (P =NS)	-2.3±7(P =0.05)
A1c	-0.37±1.1 (p=NS)	-0.52±1.1 (p=0.005)
IADL	-0.63±0.8 (p=0.007)	-0.08±0.9 (P =NS)

* between-group difference: p=0.0002

Task 5: Cerebral vascular studies at baseline, after 6 months of active intervention and 6 months of independence period. (Mos. 3-45)
SAFE laboratory at Beth Israel Medical Deaconess Medical Center

Cerebral perfusion tests including transcarnial Doppler studies, and cerebral vasoreactivity measurement evaluation. SAFE laboratory by Dr. Vera Novak

All the subjects, who were randomized to the intervention arm of the study, were given an option to sign a separate consent form for a cerebral blood flow study performed at the SAFE lab at BIDMC as per part B of the protocol. Out of 35 patients assigned to this intervention, 21 completed part B of the protocol at the baseline. Nine patients refused to sign the consent form for this additional assessment. Three patients did not have an open portal to perform vascular ultrasound. Three patients refused to undergo the test after they went to the SAFE lab and saw the testing done. Thirteen patients completed testing twice and eight patients completes all 3 times. Some subjects could not complete all the components of the study due to uncomfortable feeling and the study procedure was stopped per protocol. All the other subjects have tolerated the study procedure well.

We evaluated cerebral blood flow responses to intervention using a protocol with simultaneous beat-to-beat measurements of cardiovascular parameters and cerebral blood flow velocities at baseline and during head tilt. Vascular reserve was tested using our established CO₂ vasoreactivity protocol that included hyperventilation and CO₂ breathing. Overall, the vasoreactivity coefficient that was calculated from mean blood velocities in the right and left middle cerebral arteries (MCAR mean 0.61 ± 0.88 , MCAL- 0.92 ± 0.55 cm/s/mmHg) was lower in this population than generally observed for general population $1.29-1.34 \pm 0.16$ (Hajjar et al 2007). Over the 6 months period there was a further decline of vasoreactivity, of an unclear clinical significance. In general, there were no significant changes in mean blood flow velocities and cardiovascular parameters over the intervention period, in those with improved vs. non improved A1C control. However, at 6 months there was a negative correlation between A1C change and systolic blood pressure and mean blood flow velocity, indicating an improvement of flow velocities and a decrease in blood pressure in response to hyperventilation.

Baseline mean blood flow velocities were also lower in this cohort of diabetic participants with hypertension (33.7 ± 2.7 cm/s), as compared to non-hypertensive diabetics (40.5 ± 3.1 cm/s) and non-diabetics controls (52.9 ± 3.3 cm/s) ($p < 0.0001$).

In addition, baseline mean velocities were also lower in those with very high A1C ($> 8\%$ 9.2 ± 0.1 , $N=38$) (32.9 ± 3.5 cm/s) as compared to diabetics with lower A1C levels ($8-7\%$, 7.42 ± 0.1 , $N=23$) (36.1 ± 4.8 cm/s), low A1c ($< 7\%$, 6.24 ± 0.12 , $N=71$) (41.7 ± 3.2 cm/s) and controls with normal A1C ($< 5.7\%$, 5.35 ± 0.1 , $N=34$) (54.5 ± 4.7 cm/s) ($p=0.0035$).

In conclusion, in older diabetic patients blood flow declines significantly with uncontrolled diabetes (A1C.8%) and co-morbidities (hypertension and obesity).

We presented our interim data at the 68th annual meeting of the American Diabetes Association. We are currently performing final analysis of the data preparing for a publication. The abstract is as follows.

1. Effects of Diabetes Mellitus on Cognitive Functions in older Adults: American Diabetes Association Scientific Sessions 2008

Background: Diabetes mellitus (DM) is a complex metabolic syndrome associated with microvascular disease and regional hypoperfusion. Specifically, it appears that the fronto-temporal cortex that controls memory and decision making is the most sensitive to diabetic

metabolic disturbance. We aimed to determine the effects of DM severity, co-morbidities, body mass index (BMI), and vascular inflammation on functional outcomes in older adults.

Methods: We studied 34 subjects with type 2 DM (64.9 ± 8.9 yrs, 19 men and 15 women) and 28 healthy subjects (66.3 ± 7.8 yrs, 12 men and 16 women). Differential WBC, intracellular and vascular adhesion molecules (sICAM-1, sVCAM-1), TNF- α , IL-6, C-reactive protein (CRP) were measured. Gait speed was calculated from 12 min of hallway walking. Each subject performed a battery of neuropsychological tests to assess memory (Clock-in-the-Box; CIB, Hopkins Verbal Learning Test; HVLT, Rey-Osterreith Complex Figure; ROCF) and filled out questionnaires regarding depression (Geriatric Depression Scale; GDS) and activities of daily living (Instrumental Activities of Daily Living Scale; IADL). Data were analyzed using the least square models and ANOVA.

Results: DM group had higher BMI ($p=0.007$), GDS ($p=0.006$), IADL ($p=0.014$), and TNF- α ($p=0.006$), and lower scores on measures of memory: CIB ($p=0.005$) and HVLT retention T-scores ($p=0.039$). Age, sex, mean blood pressure (MBP), ROCF, gait speed, CRP, and other immunoassays were not different between the groups. In both groups, BMI was positively associated with GDS ($p=0.0002$), and lower HVLT score was associated with increased MBP ($p=0.01$). IL-6 was negatively associated with CIB measures of memory ($p=0.037$), and higher values of IADL ($p=0.016$). Slower gait speed indicated higher IADL ($p=0.019$) and lower HVLT retention T-score ($p=0.027$). Among diabetic subjects, higher BMI was associated with higher GDS ($p=0.0002$) and higher HbA1c ($p=0.003$), and HVLT retention T-scores were negatively associated with MBP ($p=0.004$).

Conclusions: Type 2 diabetes mellitus affects functions of short term memory and retention. High BMI and poor BP control are associated with worse DM control and functional outcomes of memory, depression and ability to perform daily activities.

Task 6: Analysis of data and information distribution. (Mos. 36-48): Joslin Clinic

We are now performing the final analysis of the longitudinal data and are in process of writing the manuscript. Our final abstract will be presented as poster in the upcoming scientific meeting of the American Diabetes Association On June 24th 2011.

1. Age-specific Barriers Assessment and Intervention via Phone Improves Glycemic Control and Functionality in Older Adults: A Randomized Controlled Study.

The American Diabetes Association guidelines recommend the assessment of both age-specific barriers and geriatric syndrome to improve diabetes management in older adults. However, the impact of such a strategy on outcomes is unknown.

Methods: We performed a randomized controlled study to evaluate the effect of assessment and intervention for age-specific barriers, implemented via phone communication between visits, on the glycemic control and other parameters in elderly subjects. Adults ≥ 69 years with $A1C \geq 8\%$ were randomized to 3 groups; group 1: attention control ($n=31$) and groups 2 & 3: intervention ($n=69$). Intervention included assessment of barriers by a geriatric diabetes team and designing strategies to improve patients' ability to follow diabetes management plans as prescribed by their providers. The interventions were implemented via phone calls by an office-based diabetes educator in group 2 ($n=34$) and by a care manager in group 3 ($n=35$). The attention control subjects received equal number of "courtesy" phone calls by an educator. All subjects underwent measurement of glycemic control (A1C), functionality (Tinnetti and 6-minute walk test -6MW), self-care inventory-revised (SCI), and diabetes-related distress (PAID).

Results: We assessed 100 patients (age 75 ± 5 , duration 21 ± 13 years, 67 % with type-2, 89% on insulin). From baseline to 6-months, the glycemic control improved in the intervention groups but not in attention control. Similarly, the measures of functionality and SCI scores

improved in intervention groups compared to control. The PAID score decreased in all 3 groups.

Conclusion: Phone communication between clinic visits by an educator aware of age-specific barriers improves glycemic control and other outcomes in older adults with diabetes.

	Changes from baseline to 6 months (Paired T-tests)			
	Group 1	Group 2	Group 3	ANOVA Between- groups
A1C	-0.34 (p=NS)	-0.5 (p<0.01)	-0.43 (p<0.01)	P = NS
SCI	1.5 (p=NS)	4.6 (p<0.009)	8.5 (p<0.0001)	P<0.01
Tinneti test	-2.5 (p<0.01)	+1.7 (p<0.03)	+0.5 (p=NS)	P<0.003
6MW	-48.7(p<0.06)	+6.4 (p=NS)	+9.4 (p =NS)	P<0.03
PAID	-6.2 (p<0.02)	-5.7 (p<0.01)	-10 (p<0.0009)	P= NS

Key Research Accomplishments

- Geriatric specific barriers assessment and interventions by phone calls with help of a diabetes educator improves glycemic control as well as functionality in older patients with diabetes. A system that provides phone call contact in-between the visits to medical provider would improve diabetes care and overall health with possible cost savings.
- High prevalence of hypoglycemic episodes are observed in older individuals even with poor glycemic control. These findings were not apparent by finger stick measurements or by patient's symptoms but were only picked up by continuous Glucose Monitoring (CGM). This finding will have important an impact on establishing A1C goals in older patients.
- Older patients even with long duration of diabetes need periodical assessment and education regarding insulin injection techniques, medication compliance, and exercise program. It is also important to assess and improve their social support system.

Reportable Outcomes:

Publications 2008-2011:

1. Angela Botts and **Medha N. Munshi**. Diabetes In the Elderly. In: Current Cardiovascular Risk Reports. Philadelphia: Current Medicine Group LLC;2008. p. 382-389
2. Alissa R. Segal, PharmD, CDE, **Medha N. Munshi**, MD. Insulin Therapy for Older Adults with Diabetes. In: Geriatrics and Aging. Toronto (Canada): Regional Geriatric Programs of Ontario;2008. p. 357-362.
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Abstracts 2008-2010

1. Emmy Suhl, Laura Desrochers, Patricia Bonsignore, Adrienne Sternthal, Judy Giusti, **Medha N. Munshi**: Higher Exercise Capacity In Older Adults With Diabetes Is Associated With Better Self-Care Ability And Less Diabetes-Related Stress. . In: American Diabetes Association 69th Annual Meeting; New Orleans La; 2009.367-OR
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Funding received based on work supported by this grant:

Graetz Foundation Grant (Joslin clinic)	6/1/2010 -5/31/2011
	\$ 50,000

Cardiac Autonomic Dysfunction in Older Adults with Diabetes
Role: PI (Medha Munshi)

Conclusion:

Our results show that phone contacts by a diabetes educator between the clinic visits to encourage management modifications based on patients ongoing barriers can improve diabetes control, functionality, and self-care, and reduce diabetes-related distress.

Our results are extremely significant as for the first time it identifies approach that may help improve diabetes control in the older adults and improve functionality that directly impacts quality of life. If our findings are confirmed in a larger study, this type of timely low cost intervention can prevent decline in patient's health and perhaps hospitalization and may provide basis for policy change for the best management of older patient with diabetes. This policy will especially be of benefit to the Veterans Hospitals as they have excellent structure already in place with availability of diabetes educators and geriatric specialists.

Other important observations from this study are as follows:

1. Older patients with diabetes have many challenges that prevent them from following their diabetes treatment properly. For example, if an elderly individual with diabetes gets sick or has a family emergency, his/her blood glucose may go too high or too low. A timely phone intervention by a diabetes educator can prevent further deterioration of the blood glucose and an adjustment in doses of medication/insulin can quickly regain better glucose control. **Thus, helping older patients to overcome obstacles in taking medications, exercising and following diet can not only improve glucose control but also improve their gait and balance, ability to do day to day activity, stress related to diabetes, and ability to do self-care.**
2. Older patients with even poor glucose control tend to get low blood glucose episodes. These low blood glucose episodes are not recognized by the patients and majority tend to occur at night between 10 pm and 6 am. **Thus, low blood glucose episodes should be carefully looked for in all older patients with diabetes in spite of their glucose control.**
3. The older patients who lack good social resources and support do worse not only with their glucose control, but also have poor exercise endurance and more frequent emergency medical visits. **Thus, it is important to encourage good social safety net in elders with diabetes.**
4. Older adults with diabetes make mistakes in insulin techniques even when they have been injecting the insulin for many years. **Thus, older patients even with long duration of diabetes need periodical assessment and education regarding insulin injection techniques and medication compliance.**
5. Older patients who have high exercise capacity are able to manage their diabetes better. **Thus, it is important to encourage exercise in all elders with diabetes.**

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List of Personnel that received salary at any point during this grant period:

Medha Munshi, MD, Principal Investigator
Adrienne Sternthal, Geriatric Life Specialist
Katie Weinger, Co-Investigator
Patricia Bonsignore, Registered Nurse, for intervention group
Judith Giusti, Educator for attention control group
Emmy Suhl, Educator for attention control group
Yishan Lee, Data Analyst
Courtney Ryan, Research Assistant

Appendix;

We have attached PDF of the publications that have acknowledged this grant as the source of funding.

Frequent Hypoglycemia Among Elderly Patients With Poor Glycemic Control

Medha N. Munshi, MD; Alissa R. Segal, PharmD; Emmy Suhl, RD; Elizabeth Staum, RD; Laura Desrochers, BS; Adrienne Sternthal, BS; Judy Giusti, RD; Richard McCartney, BA; Yishan Lee, MS; Patricia Bonsignore, MS; Katie Weinger, EdD

Background: Episodes of hypoglycemia are particularly dangerous in the older population. To reduce the risk of hypoglycemia, relaxation of the standard hemoglobin A_{1c} (HbA_{1c}) goals has been proposed for frail elderly patients. However, the risk of hypoglycemia in this population with higher HbA_{1c} levels is unknown.

Methods: Patients 69 years or older with HbA_{1c} values of 8% or greater were evaluated with blinded continuous glucose monitoring for 3 days.

Results: Forty adults (mean [SD] age, 75 [5] years; HbA_{1c} value, 9.3% [1.3%]; diabetes duration, 22 [14] years; 28 patients [70%] with type 2 diabetes mellitus; and 37 [93%] using insulin) were evaluated. Twenty-six patients (65%) experienced 1 or more episodes of hypoglycemia (glucose level <70 mg/dL).

Among these, 12 (46%) experienced a glucose level below 50 mg/dL and 19 (73%), a level below 60 mg/dL. The average number of episodes was 4; average duration, 46 minutes. Eighteen patients (69%) had at least 1 nocturnal episode (10 PM to 6 AM). Of the total of 102 hypoglycemic episodes, 95 (93%) were unrecognized by finger-stick glucose measurements performed 4 times a day or by symptoms.

Conclusions: Hypoglycemic episodes are common in older adults with poor glycemic control. Raising HbA_{1c} goals may not be adequate to prevent hypoglycemia in this population.

Arch Intern Med. 2011;171(4):362-364

Author Affiliations: Sections of Adult Diabetes (Drs Munshi and Segal and Ms Staum) and Clinical, Behavioral, and Outcome Research (Mss Suhl, Sternthal, Giusti, and Lee; Mr McCartney; and Dr Weinger), Joslin Diabetes Center, Division of Gerontology, Department of Medicine, Beth Israel Deaconess Medical Center (Dr Munshi), Harvard Medical School (Drs Munshi and Weinger), Department of Pharmacy Practice, Massachusetts College of Pharmacy and Health Sciences (Dr Segal), and Department of Health Sciences, Northeastern University (Ms Desrochers), Boston; and Diabetes Program, Valley Medical Group, Amherst (Ms Bonsignore), Massachusetts.

HYPOGLYCEMIA IN ELDERLY patients with diabetes mellitus increases the risk of cardiovascular and cerebrovascular events,¹ progression of dementia,² injurious falls,³ emergency department visits, and hospitalization.⁴ Hypoglycemic episodes are difficult to diagnose in this population and are easily missed by intermittent finger-stick measurements. Recent large studies⁵ have shown lack of benefit and sometimes higher risk of morbidity and mortality with tight glycemic control, especially in older adults. Therefore, the American Geriatric Society and the American Diabetes Association recommend relaxing glycemic control for vulnerable patients⁶ (hemoglobin A_{1c} [HbA_{1c}] <8% instead of the usual <7% [to convert HbA_{1c} levels to proportions of total hemoglobin, multiply by 0.01]). However, it is unknown whether relaxing the goal to an HbA_{1c} level of 8% or greater decreases the frequency of hypoglycemia in older patients remains unknown. Thus, we evaluated hypoglycemia in older diabetic patients with HbA_{1c} levels of 8% or greater with continuous glucose monitoring (CGM).

METHODS

Community-living patients 69 years or older seen at a tertiary care diabetes center with HbA_{1c} levels of 8% or greater were evaluated with blinded CGM (iPro; Medtronic, Inc, Northridge, California). The study was approved by the Committee on Human Subjects, and all patients provided written informed consent. Continuous glucose monitoring measured interstitial glucose levels at 5-minute intervals for a 3-day period in all patients while they continued their usual daily activities. Patients measured their glucose level by the finger-stick method 4 times a day while wearing CGM and recorded symptoms suggestive of hypoglycemia. Patients completed a demographics and treatment-related questionnaire, along with a modified clock-drawing test,⁷ Geriatric Depression Scale,⁸ Activities of Daily Living⁹ and Instrumental Activities of Daily Living,¹⁰ Six-Minute Walk Test,¹¹ Tinetti Test,¹² and Self-care Inventory-Revised.¹³

Continuous data are presented as mean (SD) when normally distributed and as median (range) when not normally distributed; frequency data are presented as number (percentage). Between-group differences in patient characteristics were compared with the Fisher exact

test for categorical variables and the Wilcoxon-Mann-Whitney test for continuous variables.

We analyzed CGM data by measuring the following: (1) total number of hypoglycemic episodes (glucose level <70 mg/dL [to convert glucose to millimoles per liter, multiply by 0.0555]); (2) nocturnal hypoglycemic episodes (10 PM to 6 AM), which are dangerous because of patients' inability to recognize and treat them; (3) hypoglycemic episodes captured by CGM but unrecognized by finger-stick monitoring or symptoms; (4) duration (longer episodes are more dangerous); and (5) severity (glucose levels of <50, <60, and <70 mg/dL).

RESULTS

Forty patients 69 years or older were evaluated. Of these, 26 (65%) had at least 1 episode of hypoglycemia (median glucose level, 63 [range, 42-69] mg/dL) during the 3-day period. The groups with and without hypoglycemia did not differ in patient characteristics, comorbidities, exercise capacity, gait/balance, self-care frequency, or diabetes-related stress (all $P > .05$) (**Table**).

Among the 26 patients with hypoglycemia, 12 (46%) had an episode with glucose levels below 50 mg/dL, and 19 (73%) had an episode with levels below 60 mg/dL. The average number of episodes was 4, with an average duration of 46 minutes. Of a total of 102 hypoglycemic episodes, 95 (93%) were unrecognized by finger-stick monitoring or by symptoms. However, only 2 patients reported "hypoglycemia unawareness" in the questionnaire. Eighteen of the 26 patients (69%) experienced 1 or more nocturnal episodes (average duration, 56 minutes). No nocturnal episodes were recognized by patients.

We evaluated CGM results by levels of glycemic control (as evidenced by HbA_{1c} level) and type of diabetes in the 26 patients with hypoglycemia. Fourteen patients had HbA_{1c} levels between 8% and 9% and 12 had HbA_{1c} levels greater than 9%; the groups did not differ in the frequency (5.0 vs 2.7), duration (3.5 vs 2.4 hours), or severity (1.2 vs 1.1 episodes with glucose levels <50 mg/dL) of hypoglycemic episodes or in the number of unrecognized episodes (2.5 vs 4.6). Similarly, 10 pa-

Table. Characteristics of Patients With and Without Hypoglycemia Detected by Continuous Glucose Monitoring

Characteristic	No. (%) of Patients		
	All Patients (N=40)	No Hypoglycemia (n=14)	≥1 Episode of Hypoglycemia (n=26)
Age, mean (SD), y	75 (5)	76 (5)	74 (5)
HbA _{1c} , mean (SD), %	9.3 (1.3)	9.6 (1.3)	9.2 (1.3)
Diabetes duration, mean (SD), y	22 (14)	22 (10)	22 (16)
Type 2 diabetes mellitus	28 (70)	12 (86)	16 (62)
BMI, mean (SD)	31 (7)	33 (7)	29 (7)
Diabetes treatment			
Insulin only	22 (55)	7 (50)	15 (58)
Insulin + oral	15 (38)	5 (36)	10 (38)
Sulfonylurea ± metformin	3 (8)	2 (14)	1 (4)
hydrochloride ± rosiglitazone maleate			
Living alone	9 (22)	4 (29)	5 (19)
No. of daily medications, mean (SD)	8.2 (4.0)	8.5 (4.0)	8.1 (4.0)
Cognitive dysfunction	10 (25)	5 (36)	5 (19)
Depression	6 (15)	4 (29)	2 (8)
Hypertension	33 (82)	13 (93)	20 (77)
Recent falls	13 (32)	4 (29)	9 (35)
Fear of falling	23 (58)	9 (64)	14 (54)
Vision problems	9 (22)	3 (21)	6 (23)
Hearing problems	16 (40)	7 (50)	9 (35)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HbA_{1c}, hemoglobin A_{1c}; ±, with or without.

SI conversion factor: To convert HbA_{1c} to a proportion of total hemoglobin, multiply by 0.01.

tients had type 1 and 16 patients had type 2 diabetes mellitus, and the groups did not differ in the frequency (4.3 vs 3.7), duration (3.2 vs 2.9 hours), or severity (1 vs 1.3 episodes with glucose levels <50 mg/dL) of hypoglycemic episodes or in the number of unrecognized episodes (3.7 vs 3.6).

We also evaluated patient characteristics according to the severity of hypoglycemic episodes. The groups with patients who experienced no hypoglycemia, hypoglycemic episodes with glucose levels below 50 mg/dL, and hypoglycemic episodes with glucose levels between 50 and 70 mg/dL did not differ in age, type of diabetes, duration of diabetes, HbA_{1c} level, treatment with insulin, presence of comorbidities, or living status.

COMMENT

This study found an unexpectedly high frequency of hypoglycemic episodes in older adults with poor glycemic control. This finding is critical in the debate concerning glycemic goals in older adults. Current guidelines⁶ based on expert opinions suggest relaxing HbA_{1c}

goals to below 8% for vulnerable elders to avoid hypoglycemia-related morbidity. In the present study, 26 of 40 patients (65%) with HbA_{1c} levels of 8% or greater experienced 1 or more hypoglycemic episodes in a 3-day period. More important, 12 of the 26 patients with hypoglycemia experienced at least 1 episode of severe hypoglycemia (glucose level <50 mg/dL). These results suggest that simply relaxing HbA_{1c} goals may not be adequate to protect frail older adults against hypoglycemia.

In our study, not only patients with type 1 but also those with type 2 diabetes mellitus and poor glycemic control had frequent hypoglycemic episodes. This new information is important in considering recommendations of glycemic goals in the rapidly growing population of older adults with type 2 diabetes. We found that finger-stick glucose testing 4 times a day did not coincide with CGM-detected hypoglycemia. Most daytime episodes and all nighttime episodes were unrecognized both symptomatically and by finger-stick glucose monitoring. These results may partially explain the low incidence of hypoglycemia reported in previous studies. We did not ob-

serve a difference in comorbidities and functionality between patients with and without hypoglycemia, perhaps because of the small sample size. The association between different classes of oral medications and/or various insulin regimens and the frequency of hypoglycemia will require larger studies.

In a recent retrospective study, Munshi and colleagues showed that simplification of diabetes regimens in older adults with diabetes is associated with decreased frequency of self-reported hypoglycemia.¹⁴ Further studies are needed to determine whether a simplified treatment regimen that better matches patients' self-care abilities also improves hypoglycemic episodes detected by CGM. Our findings raise caution for relying on HbA_{1c} as the sole measure of "good diabetes management" in elderly patients with diabetes, and we recommend careful and in-depth assessment for hypoglycemia by both patients and providers.

Accepted for Publication: September 6, 2010.

Correspondence: Medha N. Munshi, MD, Joslin Diabetes Center, One Joslin Place, Boston, MA 02215 (medha.munshi@joslin.harvard.edu).

Author Contributions: Dr Munshi had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Munshi and Suhl. *Acquisition of data:* Munshi, Segal, Suhl, Staum, Desrochers, Sternthal, Giusti, McCartney, and Bonsignore. *Analysis and interpretation of data:* Munshi, Segal, Lee, and Weinger. *Drafting of the manuscript:* Munshi and

Giusti. *Critical revision of the manuscript for important intellectual content:* Munshi, Segal, Suhl, Staum, Desrochers, Sternthal, McCartney, Lee, Bonsignore, and Weinger. *Statistical analysis:* Munshi, Lee, and Weinger. *Obtained funding:* Munshi. *Administrative, technical, and material support:* Munshi, Segal, Suhl, Staum, Desrochers, Sternthal, Giusti, McCartney, and Bonsignore. *Study supervision:* Munshi.

Financial Disclosure: None reported.

Funding/Support: This study was supported in part by grant 1-07-CR-40 from a clinical research award from the American Diabetes Association (Dr Munshi), grant W81XWH-07-1-0282 from the Department of Defense Peer-Reviewed Medical Research Program of the Office of the Congressionally Directed Medical Research Programs (Dr Munshi), and by grants from the Graetz Foundation (Dr Munshi), and grants P30 NIDDK36836 (Joslin Diabetes Center) and R01 NIDDK060115 (Dr Weinger) from the National Institute of Diabetes and Digestive and Kidney Diseases.

Previous Presentation: This study was presented in part at the 70th Annual Scientific Meeting of the American Diabetes Association; June 26, 2010; Orlando, Florida.

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Use of Serum c-Peptide Level to Simplify Diabetes Treatment Regimens in Older Adults

Medha N. Munshi, MD,^{a,b,c} Mellody Hayes, BA,^a Adrienne Sternthal,^a Darlene Ayres, RN^a

^aJoslin Diabetes Center, Boston, Mass; ^bBeth Israel Deaconess Medical Center, Boston, Mass; ^cHarvard Medical School, Boston, Mass.

ABSTRACT

BACKGROUND: Diabetes management in older adults is challenging. Poor glycemic control and high risk of hypoglycemia are common in older patients on a complicated insulin regimen. Newer oral hypoglycemic agents have provided an opportunity to simplify regimens in patients with type-2 diabetes on insulin. Serum c-peptide is a test to assess endogenous production of insulin. We analyze the use of serum c-peptide level in simplifying diabetes regimen by decreasing or stopping insulin injection and adding oral hypoglycemic agents in older adults.

METHODS: One hundred patients aged over 65 years with either poor glycemic control or difficulty coping with insulin regimen seen at a geriatric diabetes clinic were analyzed for this study. The data on serum c-peptide levels and A1c, along with demographic information, were obtained from medical charts.

RESULTS: Sixty-five of 100 patients (aged 79 ± 14 years, duration of diabetes 21 ± 13 years) had detectable serum c-peptide levels. Forty-six of 65 patients were available for simplification of regimen. Eleven of 46 patients had other co-morbidities preventing use of oral hypoglycemic agents. In 35/65 patients, simplification was completed successfully. Nineteen of 35 patients were converted to all-oral regimens (off insulin), while 16/35 had simplification of regimen by addition of oral hypoglycemic agents and lowering the number of insulin injections from an average of 2.7 to 1.5 injections/day ($P = .001$). Glycemic control improved significantly in patients with a simplified regimen ($8.0\% \pm 1.5\%$ vs $7.4\% \pm 1.5\%$; $P < .002$), and patients reported fewer hypoglycemia episodes.

CONCLUSIONS: Serum c-peptide level can be used to simplify insulin regimen in older adults with diabetes.

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KEYWORDS: c-Peptide; Diabetes; Older adults; Simplification; Treatment

With aging, patients with diabetes face an increased incidence of multiple co-morbidities.^{1,2} Some of the medical co-morbidities include cognitive dysfunction, depression, polypharmacy, and physical dysfunction. It is

difficult for primary care providers to manage diabetes in patients who have a difficulty performing self-care and following a complicated treatment regimen. Even patients who are on an insulin regimen for a substantial period of time find it difficult to cope due to the added burden of co-morbidities.³ Regimens with multiple insulin injections that require insight into the carbohydrate-insulin interaction as well as multiple finger-stick monitoring can lead to increased risk of complications such as hypoglycemia and associated falls.⁴ Thus, older adults may benefit from a simplification of their regimen. The ability of patients who have longstanding diabetes and are on insulin treatment to respond to oral hypoglycemic agents remains unclear. In this study, we evaluate use of serum c-peptide levels to guide simplification of diabetes regimen.

Funding: The study was partly supported by a grant from the DERC; NIH 5P30 DK36836-19 (MM), a clinical research award from ADA 1-07-CR-40 (MM), and Department of Defense PRMRP of the Office of the Congressionally Directed Medical Research Programs, W81XWH-07-1-0282(MM).

Conflict of Interest: All the authors declare no conflict of interest that may affect the conduct or reporting of the work submitted.

Authorship: All authors had access to the data and participated in the preparation of the manuscript.

Requests for reprints should be addressed to Medha Munshi, MD, Beth Israel Deaconess Medical Center, 110 Frances Street, LMOB 1B, Boston MA 02215.

E-mail address: medha.munshi@joslin.harvard.edu

RESEARCH DESIGN AND METHODS

We retrospectively analyzed all of the patients over the age of 65 years seen at a geriatric diabetes clinic from 2001 through 2006 in whom serum c-peptide levels were measured to identify those with endogenous insulin production. Serum c-peptide levels were measured in patients with either poor glycemic control or difficulty coping with insulin regimen. In patients with detectable serum c-peptide levels (>1.1 ng/mL; normal range 1.1–3.2 ng/mL), one or more oral hypoglycemic agents were added to simplify the regimen. Thiazolidinediones and metformin were used as insulin sensitizers in patients requiring large amounts of insulin. These medications were avoided in patients with co-morbidities that prohibit their use (eg, coronary artery disease, congestive heart failure, leg edema, renal failure). Insulin secretagogues (sulfonylurea and nonsulfonylurea compounds) were used in patients with low risk of hypoglycemia and were avoided in patients with erratic eating habits and hypoglycemic unawareness. If patients were unable to tolerate any oral hypoglycemic agents, we attempted to decrease the number of insulin injections (eg, changing the regimen from basal-bolus to mixed or longer-acting insulin twice a day). Medical and demographic information was collected from the chart.

We collected data on A1c measurements, as well as data on reports of hypoglycemic episodes at baseline and as available up to 4 consecutive visits over a period of up to 1 year following regimen change from the chart notes. Any episodes of hypoglycemia in the past 6 months were considered positive for the purpose of history. The study was reviewed by the committee on human subjects and was found to be exempt.

STATISTICAL METHODS

We calculated descriptive statistics and frequency distributions for all variables. Data are presented as mean \pm SD for continuous data and as n (%) for frequency data. The differences between clinical and demographic variables were compared between patient groups before and after simplification of regimen using the unpaired *t* test for discrete or continuous data and the chi-squared test for frequency distribution. Within-group changes from baseline in A1c were analyzed using the *t* test for paired data. A value of $P < .05$ was considered to indicate statistical significance.

RESULTS

Sixty-five of 100 older adults had detectable serum c-peptide levels. The average age of these patients was 80 ± 6 years

(range 67–93 years), and 65% of the patients were women. Patients were taking 8.7 ± 4 medications/day (range 3–16) and the mean duration of diabetes was 20.8 ± 12.5 years (range 1–50 years). Thirty-seven of 65 patients reported hypoglycemic episodes during their office visit. The Table shows characteristics of patients with detectable serum c-peptide levels and patients who had successful simplification of regimen.

The treatment regimen was not simplified in 19 of 65 patients with detectable c-peptide levels; 9 patients preferred to remain on insulin (did not want to add oral medications) and 10 patients were lost to follow-up before changes could be instituted. Of 46 patients available for simplification of regimen, 11 patients were unable to use oral hypoglycemic agents due to presence of multiple co-morbidities. Regimen was successfully modified in 35 patients. Metformin was added in 14 patients, sulfonylurea was added in 16 patients, and thiazolidinediones were added in 19 patients. Twenty-three patients had one oral agent added,

while 8 patients needed 2 oral agents and 4 patients were on 3 oral agents (median: 1 oral agent/patient; range: 1–3). Of these, the insulin therapy in 19 patients was completely discontinued and patients were maintained only on oral hypoglycemic agents. In the other 16 patients, an oral hypoglycemic agent was added and the number of daily insulin injections was decreased from an average of 2.7 ± 1 to 1.5 ± 0.8 injection/day ($P = .001$). In 3 of the patients, glycemic control deteriorated on oral medications, and once-daily long-acting insulin was added.

CLINICAL SIGNIFICANCE

- Older adults with long duration of diabetes, on insulin therapy, may have preserved endogenous insulin production as seen by detectable serum c-peptide level.
- Serum c-peptide levels can be used to guide simplification of the diabetes regimen in older adults who have difficulty coping with a complicated insulin regimen.
- The simplification of the diabetes regimen may lead to reduced risk of hypoglycemia without compromising glycemic control.

Table Characteristics of Patients with Detectable Serum c-Peptide Levels and Patients Who had Successful Simplification of Regimen

	All Patients with Detectable c-Peptide	Patients with Successful Simplification of Regimen
Number	65	35
Age (years)	80.2 ± 6	80 ± 6
Sex (M/F)	23/42	13/22
Duration of diabetes	21 ± 13	19 ± 12
Average c-peptide	2.3 ± 1	2.43 ± 1.2
No. of medications/day	8.7 ± 4	8 ± 4
No. of insulin injections/day	2.5 ± 1	2.6 ± 1
No. of patients reporting hypoglycemia (%)	55	63

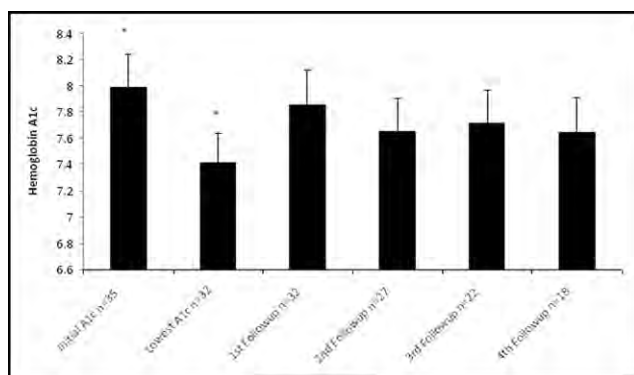


Figure A1c at the initial visit, at the lowest level, and at up to 4 consecutive visits in 1 year following simplification of regimen. * $P < .002$.

Among the 35 patients whose regimen was simplified, initial A1c, before change in the regimen, was $8.0\% \pm 1.5\%$, compared with $8.1\% \pm 1.4\%$ in patients whose regimen could not be simplified. In patients with simplified regimen, we evaluated the excursion of A1c as available during 4 consecutive visits over a period of up to 1 year following addition of oral hypoglycemic agents (Figure). The number of subjects at the initial A1c measurement was 35, and the subsequent measurements were 32, 27, 22, and 18, respectively. A1c improved from a pre-intervention level of $8.0\% \pm 1.5\%$ to $7.4\% \pm 1.5\%$ at the lowest level ($P < .002$). In 3 patients, follow-up A1c was not available after the changes were made. Although this was not a randomized study, the patients whose regimen was not simplified had their A1c change from $8.1\% \pm 1.4\%$ initially to $7.8\% \pm 1.4\%$ at the lowest level ($P = \text{not significant}$).

Eleven of these patients had A1c $>8\%$, while 22 patients had A1c $\leq 8\%$ at the time of serum c-peptide measurement. Following modification of the regimen, improvement in A1c was observed in the group with high A1c ($9.3\% \pm 1.5\%$ to $8.2\% \pm 1.8\%$; $P < .0001$); while in the group with lower A1c, the favorable A1c was maintained ($7.0\% \pm 0.8\%$ to $6.9\% \pm 1\%$; $P = \text{not significant}$).

Before simplification of the regimen, 22 of 35 patients reported episodes of hypoglycemia during their office visit. Following simplification of the therapy, report of hypoglycemic episodes significantly decreased, with only 2 patients reporting such episodes.

DISCUSSION

This study shows that a majority of older adults with long duration of diabetes have preserved endogenous production of insulin. In addition, we have shown successful utilization of detectable serum c-peptide levels to simplify treatment regimen. Such change in the study population decreased the reported episodes of hypoglycemia, and maintained or improved their glycemic control.

Many older adults have long duration of diabetes and were started on insulin regimen early on. Although most older patients have type-2 diabetes, primary care providers usually feel uncomfortable trying oral medications in patients with long duration of diabetes and face difficulties in patients who are unable to perform self-care. In recent years, with the introduction of new oral hypoglycemic agents, more options are available.⁵⁻⁷ However, there is currently a lack of data about the type of patient that can be safely converted to a simpler regimen or an effect of the change on glycemic control. Serum c-peptide levels can be used as a simple tool in such situations. Due to the retrospective nature of the current study, it is not possible to attribute the improvement in A1c to regimen change; however, it was reassuring to see that glycemic control did not deteriorate after simplification. It is likely that improvement in A1c seen in patients with simplified regimen is due to their ability to better cope with the simplified treatment.

A major concern for older adults with diabetes is the risk of hypoglycemia. In a recent study, older patients on insulin had a higher risk of falls with tighter control.⁸ Falls lead to fractures and decreased functionality, directly affecting quality of life in this age group.⁹ If a simplification of regimen can lower the risk of hypoglycemia as shown in this study, it may lead to significant cost-saving and improvement in quality of life.

The limitation of this brief report is its retrospective nature. However, this is an important observation and provides rationale for future prospective randomized studies to develop specific protocols and guidelines to simplify diabetes regimen in older adults.

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Cognitive and Psychosocial Aspects of Caring for Elderly Patients With Diabetes

Isao Iwata, MD, PhD, EdM, and Medha N. Munshi, MD

Corresponding author

Medha Munshi, MD
Harvard Medical School, Joslin Geriatric Diabetes Programs,
Beth Israel Deaconess Medical Center, 110 Francis Street, LMOB
1B, Boston, MA 02215, USA.
E-mail: mmunshi@bidmc.harvard.edu

Current Diabetes Reports 2009, 9:140–146
Current Medicine Group LLC ISSN 1534-4827
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The population is aging in the United States as well as worldwide. The prevalence of diabetes increases with increasing age. To provide optimal care to older adults with diabetes, unique psychosocial barriers need to be considered by medical providers. Unlike in younger adults, cognitive dysfunction/dementia and depressive mood disorders are common coexisting conditions in older adults with diabetes. This article reviews recent literature on epidemiology and clinical implications of cognitive and psychosocial dysfunctions in older patients with diabetes. This article focuses on cognitive dysfunctions, dementia, depression, and other psychosocial stresses, and their implications in the care of older adults with diabetes.

Introduction

Diabetes is a major cause of morbidity and mortality among older adults. The current prevalence of diabetes among adults 65 years of age or older is 15.3%, and 6.9% of additional individuals are thought to have undiagnosed diabetes [1•]. The group of adults with diabetes who are 75 years of age and older is the fastest growing population among all age groups with diabetes [2]. Older adults with diabetes have multiple coexisting conditions and some of them interfere with patients' ability to perform self-care. Dementia/cognitive dysfunction and depression/depressive mood are such conditions found commonly in older adults with diabetes [3–6]. The association between diabetes and these conditions has been studied for the past several decades through epidemiologic analyses and pathophysiologic investigations.

In this article, we review recent literature on epidemiology and clinical aspects of cognitive and psychosocial dysfunction in older patients with diabetes mellitus, focusing on the cognitive dysfunctions, dementia, depression, and depressive mood disorders. We also review the relevance of these cognitive and psychosocial problems on clinical management of diabetes in older patients.

Cognition and Diabetes

Cognitive impairment and diabetes

Several clinical studies have shown that diabetes is associated with cognitive impairment, and that the presence of diabetes accelerates cognitive decline in older adults [6–9]. Multiple case-control studies have assessed cognitive dysfunction using various batteries of neuropsychiatric testing. Some of these studies also assessed whether specific areas of cognitive function were affected by diabetes. Stewart and Liolitsa [6] summarized more than 20 case-control studies and found that the deficit in the attention/concentration domain and verbal fluency among patients with diabetes appeared to be consistent. However, the authors thought that the reliability of the case-control studies was somewhat questionable due to inadequate control for potential confounding factors, such as hypertension and depression. In addition, because of smaller sample size, typically involving 30 to 40 individuals, some case-control studies did not have enough power to detect small differences in cognitive function tests, leading to conflicting results.

Following the case-control studies above, several population-based studies investigated the possibility of preferential defects in cognitive function among the population with diabetes [8,10,11]. These population-based cohort studies included a large number of prescreened individuals and followed them prospectively. The Framingham study observed 187 patients with type 2 diabetes and 1624 individuals without diabetes for 28 to 30 years [10]. The authors found that type 2 diabetes was associated with a 1.8-fold increase in the risk of poor performance in visual memory in patients who also had hypertension. The longer duration of diabetes

was associated with an increased risk of poor performance in verbal memory and concept formation in the patients with diabetes. Arvanitakis et al. [11] followed 824 older Catholic nuns, priests, or brothers for a mean of 5.5 years and found that diabetes was associated with a 44% greater rate of decline in perceptual speed but not in other cognitive systems. In a recent population-based cross-sectional study, 882 older patients without dementia were enrolled. The results showed that diabetes was associated with poor semantic memory and perceptual speed controlling for age, sex, and education, although the association of diabetes with perceptual speed was not significant when controlling for vascular variables, such as congestive heart failure, current smoking, and systolic and diastolic blood pressure [12]. A recent cross-sectional study of homebound older people by Qiu et al. [13•] showed that older people with diabetes scored significantly lower in visuospatial functions and executive functions compared to peers without diabetes (Block Design test mean score \pm SD, 17.1 ± 8.6 vs 20.5 ± 9.6 ; $P = 0.003$; Trail Making Part B test median seconds to accomplish the task, 255 vs 201; $P = 0.03$).

A series of longitudinal cohort studies also have shown diabetes as a strong risk factor for cognitive decline (Table 1) [14–16]. In these studies, diabetic subjects had greater risk for cognitive decline as measured by scores on selected neuropsychological test battery, with odds ratios of 1.3 to 1.7. These longitudinal cohort studies typically used two to five different cognitive tests, but the main conclusions were often drawn from the composite scores of multiple tests. Frequently used cognitive tests that have produced a statistically significant difference between subjects with and without diabetes include the following: Digit-Span [8,14], Delayed Word-List Recall [9,14], Trail Making Part B test [7,17,18], Auditory Verbal Learning test [7], and Digit Symbol test [7,8,18]. Many studies found no significant change in scores on the Mini-Mental State Examination (MMSE) or modified MMSE [7,18], with a few exceptions [9], suggesting that MMSE may not have enough sensitivity to capture the difference in cognitive decline in a relatively short period of time (2–4 years). For assessing global cognitive function, Telephone Interview for Cognitive Status, which was modeled on MMSE, was used in the Nurses' Health Study, Women's Health Study, and Physicians' Health Study and appeared to be quite sensitive [14,15]. In older adults with diabetes, coexisting hypertension was associated with accelerated decline in cognitive and physical function [19,20]. In summary, cognitive dysfunction is commonly associated with diabetes in older adults.

Glycemic control and cognitive dysfunction

Several longitudinal studies have found that longer duration of diabetes and treatment with insulin are independently associated with a higher risk of cognitive dysfunction. Due to scarce sampling of glucose level and

unavailability of the value of hemoglobin A_{1c} (HbA_{1c}), the relationship of cognitive function and glycemic control was not addressed in those large population studies. However, in a smaller study, Munshi et al. [21•] reported that the cognitive dysfunction was associated with poor glycemic control in older adults. Similarly, van Harten et al. [22] showed that the duration of diabetes was associated with the domain motor speed in 92 older adults with type 2 diabetes. They also found that higher HbA_{1c} was associated with global cognitive dysfunction, using the HIV Dementia Scale [22]. Perlmutter et al. [23] also reported that cognitive performance was poorer in diabetic patients with elevated HbA_{1c} levels, and the authors suggested that significant cognitive impairment might complicate adherence to treatment regimen.

Some clinical trials have shown that improving glycemic control may lead to cognitive improvement in a few domains. Ryan et al. [24] showed that after 24 weeks of treatment with glyburide or rosiglitazone, working memory improved in the two treatment groups. Although such findings may suggest reversible cognitive dysfunction secondary to hyperglycemia or hyperinsulinemia, other studies suggest that most of the cognitive impairment would accumulate over time and result in irreversible structural abnormality in the brain [22].

Thus, growing evidence exists that cognitive dysfunction is associated with poor glycemic control. However, more studies are needed to assess whether improved glycemic control can lead to improved cognitive function.

Vascular dementia, Alzheimer's disease, and diabetes

Diabetes is a major risk factor for cardiovascular diseases, and is strongly associated with the development of vascular dementia that is due to macro- and/or micro-cerebrovascular angiopathy. Alzheimer's disease, a progressive brain disorder with gradually developing memory loss, inability to learn, reason, make judgments, communicate, and perform daily activities, is the most common form of a degenerative type of dementia in the United States [25]. The association of Alzheimer's disease with diabetes is not well established [26,27].

A meta-analysis of five prospective observational studies looking at the risk of all causes of dementia in patients with diabetes showed that the overall risk for developing future dementia was 1.6-fold (95% CI, 1.4–1.8) in patients with diabetes compared to those without diabetes [28]. Although patients with diabetes had a 2.2- to 3.4-fold higher risk of developing vascular dementia, the reported risk of developing Alzheimer's disease was somewhat smaller at 1.2- to 2.3-fold. This discrepancy was thought to be due to different diagnostic criteria used in these studies for Alzheimer's disease and for diabetes. Another limitation of these longitudinal studies is the lack of detailed clinical information on diabetes, such as glycemic control, treatment modality, and diabetic complications [11,26,27].

Table 1. Summary of longitudinal cohort studies for the association of diabetes and cognitive function

Study	Participants, <i>n</i>	Age, <i>y</i>	Follow-up, <i>y</i>	Diabetes ascertainment	Number with diabetes	Hypertension	Depression*	Cognitive tests showed faster decline in patients with diabetes than in those without†
Wu et al. [9]	1789	≥ 60	2	FPG ≥ 126 mg/dL, or antidiabetic medication use, or self-report	585	Controlled	Controlled (CES-D)	Modified MMSE
Hassing et al. [8]	274	80–93	6	FPG ≥ 6.7 mmol/L	36	Not controlled	Not controlled	MMSE, Symbol Digit (psychomotor speed), Verbal Meaning (semantic memory), Memory-in- Reality (episodic memory)
Logroscino et al. [14]	16,596	70–81	2	Self-report	1248	Controlled	Controlled (antidepress- sant use, mental health index, and energy-fatigue index from SF-36)	Telephone Interview for Cognitive Status (modeled on MMSE)
Kuo et al. [20]	2802	65–94	2	Self-report	358	Controlled	Not controlled	Digit Symbol Substitution Test (motor speed of processing)
Arvanitakis et al. [11]	824	> 55	5.5	Antidiabetic medication use, or self-report	127	Not controlled	Not controlled	Symbol Digit Modalities Test, Number Comparison (perceptual speed)
Okereke et al. [15]	12,233	40–84 (PHS), ≥ 45 (WHS)	4	Self-report (validation studies: 99% accuracy)	553 men, 405 women	Controlled	Controlled (self-report, history of depression)	Telephone Interview for Cognitive Status

*Case ascertainment.

†Assessed area of cognitive function.

CES-D—Center for Epidemiologic Studies-Depression; FPG—fasting plasma glucose; MMSE—Mini-Mental State Examination; PHS—Physicians' Health Study; SF-36—Short-Form Health-Related Quality-of-Life Questionnaire; WHS—Women's Health Study.

The possible mechanisms of association between diabetes, cognitive dysfunction, and dementia have been discussed and summarized in recent review articles [25]. Some of the mechanisms include direct toxicity of chronic hyperglycemia through various pathways (advanced glycation end product, polyol pathway, oxidative stress, amyloid deposition), involving different targets (blood vessels and white matter). Hyperinsulinemia is reported as another risk factor of Alzheimer's dementia because insulin may impair the clearance of amyloid β in the brain [29]. Thus, diabetes increases risk of dementia in older adults mediated by various mechanisms.

Psychosocial Aspects

Depression and diabetes

Depression and diabetes are common conditions among older adults. Based on the assessment methods used, the prevalence of depression in elderly patients with diabetes varies. In a large study by Bell et al. [3], 21.0% of older Native Americans were found to have depressive symptoms, whereas 14.6% of older African Americans and 13.6% of white Americans had depressive symptoms. A meta-analysis of 39 studies demonstrated that major depression and elevated depressive symptoms were present in 11% and 31% of individuals with diabetes, and that the prevalence of depression was higher in subjects with diabetes than in those without diabetes (OR = 2.0; 95% CI, 1.8–2.2) [30]. Studies also have shown that having depressive symptoms is a risk factor for developing type 2 diabetes [31] and that diabetes is associated with increased risk of depressive symptoms [32•]; thus, the association between diabetes and depressive symptoms is likely to be bidirectional [33•].

A meta-analysis by Lustman et al. [5] included 26 cross-sectional studies that assessed the association between glycemic control and depression. The authors showed that depression was significantly associated with higher glycohemoglobin, with the standardized effect size of 0.17, which was in the small-to-moderate range [5]. In another study, Maraldi et al. [32•] reported that among 70- to 79-year-old persons, the risk of depression and depressive mood was especially higher in those with poor glycemic control.

Depression in older patients with diabetes has a significant impact on patients' mortality [34], quality of life [35], and the health care costs to society [36]. In a 3-year prospective cohort study, Katon et al. [34] showed that older patients with diabetes and minor depression had a 1.7-fold increase in mortality and those with major depression had a 2.3-fold increase in the risk of mortality compared to patients without depressive symptoms. Patients with diabetes and depression had significantly lower scores in every dimension of the Short-Form Health-Related Quality-of-Life Questionnaire (SF-36) than those with diabetes

but no depression [35]. Among Medicare patients with diabetes, major depression was associated with 21% greater annual nonmental health-related payments than those without major depression [36].

For patients with diabetes and depression, treatment with cognitive behavioral therapy [37] and selective serotonin reuptake inhibitors [38,39] has been used successfully to manage symptoms. Interestingly, the fluoxetine treatment group in this study [38] had greater improvement in mean glycohemoglobin level. However, the difference did not reach statistical significance, partly because of relatively short treatment periods (8 weeks) [38]. Sertraline's efficacy also has been tested in clinical trials in patients with diabetes and major depressive disorders. In the trial comparing sertraline with placebo as maintenance treatment for those who achieved depression recovery with open-label sertraline treatment, the 1-year nonrecurrence rate was 66% in the sertraline group compared with 47.9% in the placebo group [39]. The clinical trial showed significant improvement in HbA_{1c} after 8 weeks of induction therapy. At the end of the randomized period, however, no difference in glycemic control occurred between the sertraline group and the placebo group, although HbA_{1c} remained low in the two groups [39]. Another interesting finding in this study was that younger age was an independent predictor of depression recurrence. The secondary analysis by Williams et al. [40] demonstrated that sertraline was not effective in preventing recurrence of depression in patients 55 years of age or older. Bogner et al. [41] conducted a multisite, practice-randomized control trial to assess the efficacy of a primary care-based depression management program for depressed patients with diabetes. They found a 51% decrease in mortality (95% CI, 2–76) in the intervention group during the 5-year follow-up. The data on glycemic control were not available in this study.

Thus, diabetes and depression have a bidirectional relationship with increased risk. Depression treatment can be successful in patients with diabetes, although its affect on glycemic control remains unclear.

Other psychosocial aspects and diabetes

Diabetes self-management imposes specific physical and emotional burdens on patients with diabetes. Delahanty et al. [42] studied the affect of treatment of diabetes on the Problem Areas in Diabetes (PAID), a 20-item self-report measure of diabetes-related emotional stress. The results showed that PAID scores were significantly higher among insulin-treated patients compared with patients on oral hypoglycemic agents or those treated with diet alone. The two most serious problems among PAID items were “worrying about the future” and “guilt/anxiety when... off track with diabetes.” Higher PAID scores (ie, greater emotional distress) were correlated with younger age, non-white race ethnicity, female gender, higher HbA_{1c}, higher

body mass index, and treatment type. Nakahara et al. [43] investigated the causal relationship between HbA_{1c} and psychosocial factors captured by the Multi-Dimensional Diabetes Questionnaire. A survey was conducted on 256 Japanese adults with type 2 diabetes (mean age, 62 years) observed at a medical center. The study results showed that self-efficacy directly reinforced adherence, and better adherence was associated with better glycemic control measure at follow-up HbA_{1c}. A qualitative research conducted by Schoenberg and Drungle [44] highlighted that psychosocial barriers to diabetes management among older adults with diabetes included financial challenges, lack of access to quality care for diabetes, and pain and disability that inhibit self-care behaviors.

In general, very old or frail elderly patients with diabetes are likely to lose physical, mental, or psychosocial independence, which requires significant involvement of caregivers in diabetes management. Caregiver stress is one area that needs to be addressed in future research. An evaluation of the social and financial support system for all older patients with diabetes should be assessed.

Relevance to Diabetes Care

Coexisting medical comorbidities are important to recognize as barriers to good glycemic control in older adults with diabetes. Cognitive dysfunction, depression, and other psychosocial issues can lead to not only poor control but also lower quality of life and increased caregiver needs, leading to higher medical expenditure in care of these patients. The All Wales Research into Elderly diabetes study found that patients with diabetes and cognitive dysfunction (MMSE score < 23) were less independent and less likely to be involved in diabetes self-care and monitoring [45]. A low MMSE score was also associated with reduced activities of daily living, and increased need for assistance in personal care. Depression also poses a great challenge in managing diabetes among older adults. Lin et al. [46] showed that major depression was associated with less physical activity, unhealthy diet, and lower adherence to medications.

Thus, it is important to 1) screen all older patients with diabetes periodically for cognitive dysfunction, depression, and other psychosocial stresses in the clinical practice; 2) individualize the management goals and plans based on the barriers when identified; and 3) optimize cardiovascular risk factors to lower the risk of vascular dementia.

Screening for psychosocial barriers

The presence of cognitive dysfunction and depressive symptoms is frequently overlooked in the care of elderly patients. It is essential to recognize early signs of cognitive decline and subtle symptoms of depression using appropriate screening tools [4].

Cognitive function screening should cover global cognitive functions, including memory and executive function.

However, the tools need to be short and easy to use in a clinical practice. MMSE is a useful screening tool that covers orientation, registration, attention, recall, language, and praxis. However, MMSE is not a sensitive test to measure executive dysfunction, which presents with subtle symptoms. The clock drawing test is another commonly used screening tool for cognitive dysfunction especially affecting executive functions. Participants are asked to draw a clock face on a paper and place the hour and the minute hands at a set time [21,45]. Because any type of cognitive assessment relies heavily on the ability to listen, read, and write, it is important to take into account any physical disability (vision, hearing, and dexterity), education, and literacy level, and the language barrier for non-native speakers.

For depressive symptoms, the 15-item Geriatric Depression Scale is a reliable and commonly used tool [4,21]. A total score above 5 suggests depressive symptoms. It is also important for clinicians to look for reversible conditions that may cause or exacerbate cognitive dysfunction and/or depressive symptoms, such as hypothyroidism, infections, metabolic abnormalities, and delirium [4]. PAID can be used for assessing diabetes-related emotional distress, although its negative correlation with age may raise questions about its sensitivity in elderly persons [42].

Individualized management for patients with diabetes and cognitive and psychosocial problems

Cognitive impairment, depression, and other psychosocial issues may interfere with the older patients' ability to perform self-care. These conditions may present as nonadherent to medical treatment or as sudden deterioration of glycemic control with no obvious causes. In each individual case, health care providers must identify unique problems and barriers in physical, cognitive, and psychosocial aspects. Depression and depressive symptoms should be treated promptly by medical therapy and/or cognitive behavioral therapy. When elderly patients exhibit significant cognitive impairment, referral to specialists for detailed neuropsychiatric evaluation may help patients and caregivers deal with this chronic and often progressive neuropsychiatric disorder. Physicians should accommodate therapeutic modality to patients' cognitive and physical capacity, and may need to change the target glycemic control to minimize the risk of hypoglycemia. A multidisciplinary team approach—clinical diabetes educators, dietitians, clinical pharmacist, social worker, endocrinologists, and primary care providers—can help improve the care for older adults with diabetes.

Optimize cardiovascular risk factors to prevent vascular dementia

A randomized control study showed that blood pressure-lowering treatment with perindopril and indapamide (mean follow-up, 3.9 years) was associated with reduced risk of dementia and cognitive decline (relative risk, 19%

[95% CI, 4–32]) [47]. Cholesterol lowering with statins also may be beneficial for preventing cognitive impairment [48]. However, no randomized clinical trials have tested the efficacy of diabetes treatment on preventing cognitive impairment and dementia. Two trials were found in clinical trial registry (<http://ClinicalTrials.gov>). One uses metformin for overweight persons 50 to 90 years of age and assesses the change in cognitive function in 12 months (ClinicalTrials.gov Identifier: NCT00620191). The other trial is the ACCORD-MIND (Action to Control Cardiovascular Risk in Diabetes—Memory in Diabetes) (ClinicalTrials.gov Identifier: NCT00182910) [49]. In this trial, the primary aim is to test whether there is a difference in cognitive decline and structural brain change in patients with diabetes who were treated with standard care compared with those treated with intensive care (target HbA_{1c} < 6.0%). Although this study will provide further insight into the association of diabetes and cognitive dysfunction, its ambitious glycemic control target (HbA_{1c} < 6%) may hinder a favorable effect on maintaining cognitive function by increasing clinical or subclinical hypoglycemia.

Conclusions

In older adults, cognitive impairment and depression are prevalent and strongly associated with diabetes. Diabetes is a major risk factor for developing cognitive dysfunction and vascular dementia. The association between diabetes and depression is bidirectional: diabetes increases the risk of depression and depressive symptoms, and patients with depression have a higher incidence of new-onset diabetes. Depression in older adults with diabetes can be treated successfully with selective serotonin reuptake inhibitors and cognitive behavioral therapy, and remission of depressive symptoms with antidepressant may lead to improved glycemic control. Because significant cognitive decline has been seen in elderly patients with diabetes and hypertension, optimizing cardiovascular risk factors is important for preventing cognitive deterioration in older patients with diabetes. Whether better glycemic control alleviates depressive symptoms or prevents cognitive impairment remains to be seen in forthcoming clinical trials. It is imperative for health care providers to periodically screen older patients with diabetes for cognitive dysfunction, depression, and other psychosocial stresses to individualize the management goals and plans.

Acknowledgments

The work was partly supported by a clinical research award from the American Diabetes Association, 1-07-CR-40 (for Medha Munshi), and a grant from the Department of Defense Peer Reviewed Medical Research Program of the Office of the Congressionally Directed Medical Research Programs, W81XWH-07-1-0282 (for Medha Munshi).

Disclosure

No potential conflicts of interest relevant to this article were reported.

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